

**REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

**I. CLAIM STATUS AND AMENDMENTS**

Claims 1-19 were pending in this application when last examined and stand rejected.

Claims 1-3, 8-10, 15-16 and 19 were examined on the merits and stand rejected.

Claims 4-7, 11-14, 17 and 18 were withdrawn as non-elected subject matter.

Claims 1-19 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional on any cancelled subject matter.

New claims 20-40 have been added to replace old claims 1-19. The language in the new claims corresponds to that in the old claims, but has been improved upon to better conform to English grammar form. Such revisions are non-substantive and not intended to narrow the scope of protection.

New claims 20, 21, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 36, 38, 39 and 40 correspond to claims 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19, respectively. Further support for new claims 20, 28, and 36 can be found in original claims 2, 9, and 16, and, for example, at page 7, lines 22-24 and 31-32, in the disclosure as filed. Further support for

new claims 22, 30, and 39 can be found in original claims 2, 9, and 16, and, for example, at page 6, lines 20-25, in the disclosure as filed.

No new matter has been added by the above claim amendments.

Claims 20-40 are pending upon entry of this amendment.

Attached herewith is a substitute Specification (both clean copy and a marked-up copy) with editorial revisions to better conform to US practice. No new matter has been added.

## **II. CLAIM OBJECTIONS**

Claims 10 and 15 were objected to for minor informalities for the reasons in items 5-6 on page 2 of the Office Action. The present amendment overcomes this objection. The new claims use language that remedies the stated bases of the objection. Withdrawal of the objection is therefore solicited.

## **III. OBJECTIONS TO THE SPECIFICATION AND THE SEQUENCE LISTING**

In items 8-10 on pages 3-4 of the Office Action, the specification was objected for containing minor informalities, including omitting headings consistent with U.S. patent practice. The Office also objected to the Sequence Listing on the basis that amino acid sequence identified as SEQ ID NO: 2 on page 6 of the disclosure is inconsistent with SEQ ID NO: 2 in the Sequence Listing.

First, it is respectfully submitted that the attached substitute Specification corrects the objections noted by the Office as it includes appropriate section headings and a Brief Description of the Drawings.

Second, with respect to the Sequence Listing, kindly note that the responses filed November 21, 2007 and October 17, 2007 should obviate this concern.

As stated in the October 17, 2007 response, the originally filed specification (at page 6, line 20) erroneously indicated a 13-40 fragment (SEQ ID NO: 2), instead of the 13-39 fragment of the HARP factor as otherwise disclosed and claimed. Applicants then amended the specification at page 6, line 22, by way of the October 17, 2007 response, to correct this inadvertent error.

In the November 21, 2007 response, Applicants submitted a revised substitute Sequence Listing in paper and computer readable form (CRF). The revised Sequence Listing contained the correct SEQ ID NO: 2, wherein the extra "T" at the end of SEQ ID NO: 2 was removed. Accordingly, SEQ ID NO: 2 in the paper copy and the CRF of the Sequence Listing submitted November 21, 2007 corresponds to the correct description of SEQ ID NO: 2 at page 6, line 22 of the disclosure as revised per the October 17, 2007 response.

Thus, it is respectfully submitted that the responses filed November 21, 2007 and October 17, 2007 fully address and overcome the objection to the Sequence Listing.

Therefore, withdrawal of the above-noted objections is solicited.

#### **IV. INFORMATION DISCLOSURE STATEMENT**

In item 11 on page 4 of the Office Action, it was indicated that the references listed at the end of the specification will only be considered if cited as part of an Information Disclosure Statement (IDS) or by the Examiner on form PTO-892.

Applicants will consider submitting such references in due course in an IDS for official consideration, if deemed appropriate.

In item 12 on page 4 of the Action, it was indicated that the references cited in the IDS of May 2, 2005 have not been considered, because the Office does not have copies of the references. It is noted that the Examiner has cited certain of these references in the PTO-892 form attached to the Office Action.

In reply, attached herewith are copies of the cited references for official consideration by the Office. Please consider the references and return an Examiner-initialed PTO 1149 form indicating such.

**V. REJECTION FOR NON-STATUTORY SUBJECT MATTER**

In item 14 on page 4 of the Office Action, claims 1 and 2 were rejected under 35 U.S.C. § 101 for being directed to non-statutory matter.

It is noted that the claims have been amended along the lines suggested by the Examiner, thereby obviating this rejection. Withdrawal of the rejection is therefore solicited.

**VI. ENABLEMENT AND WRITTEN DESCRIPTION REJECTIONS**

In item 16 on pages 4-9 of the Office Action, claims 1-3, 8-10, 15-16 and 19 were rejected under 35 U.S.C. § 112, first paragraph, for not complying with the enablement requirement.

In item 17 on pages 9-14 of the Office Action, claims 1-3, 8-10, 15-16 and 19 were rejected under 35 U.S.C. § 112, first paragraph, for not complying with the written description requirement.

Applicants respectfully traverse these rejections as applied to the new claims. The rejections will be addressed together below.

First, the enablement rejection.

In the paragraph bridging pages 4-5 of the Office Action, it was indicated that the specification is enabling for an isolated peptide consisting of SEQ ID NO: 2 or SEQ ID NO: 3, compositions comprising the isolated peptide consisting of SEQ ID NO: 2, and SEQ ID NO: 3, or SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4 and

a pharmaceutical acceptable carrier for inhibiting HARP induced angiogenesis. It was further indicated that claims 1-3, 8-10, 15-16 and 19 were not enabled, because they relate to peptides other than peptides consisting of SEQ ID NOs: 2 and 4.

In reply, kindly note that the claims have been amended in such a way as to be directed to peptides consisting of a sequence at least 90% identical to SEQ ID NOs: 2, 3 or 4. In other words, the amended claims relate to peptides consisting of very specific fragments of the HARP factor, and comprising at most three differences compared to SEQ ID NOs: 2, 3 and 4.

It is respectfully submitted that the revised new claims pertain to a limited number of peptides, and that it would not amount to undue experimentation for the skilled artisan to practice the invention in view of the guidance in the disclosure and the knowledge in the art.

In this regard, it is well established that the test of enablement is whether one reasonably skilled in the art could make or use the invention based on the disclosure in the specification coupled with the knowledge in the art without undue experimentation. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. In fact, the test is not merely quantitative, since a considerable amount of experimentation is

permissible, if it is merely routine, or if the specification provides reasonable guidance with respect to the direction in which the experimentation should proceed. See, M.P.E.P. § 2164.01 and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the instant case, it is respectfully submitted that the disclosure provides sufficient guidance to enable the scope of the limited number of peptides of the new claims.

Applicants wish to emphasize that the specification provides guidance, for example, from page 7, line 30 to page 8, line 14, as to which specific mutations within SEQ ID NOs: 2, 3 and 4 are expected not to abolish the biological activity of the peptides. In addition, the specification contains a detailed description of several well-known methods for testing whether a peptide has the biological activity recited in the functional language of the claims. See, for instance, the disclosure from page 6, line 31 to page 7, line 20.

It is respectfully submitted that the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, could construct any of the limited number of peptides encompassed by the new claims and then use the assays disclosed in the specification in order to confirm that such peptides have the requisite angiogenesis inhibiting activity and a capacity for binding to the ALK receptor. Moreover, such could be done using

the routine techniques and procedures disclosed in the specification without undue experimentation.

Further, it is noted that the references relied upon by the Office as evidence of the alleged unpredictable nature of the art are not pertinent for the newly claimed peptides nor the rejections.

In this regard, Zhang et al. teaches that peptides consisting of amino acids 1-40 and 101-136 of HARP have no angiogenesis inhibiting activity. In contrast, the present claims pertain to peptides consisting of sequences at least 90% identical to amino acids 13-39 and 111-136 of HARP. Further, as discussed in the disclosure (see for instance, page 4, line 23-25 of the original application), Applicants surprisingly found that such peptide fragments of HARP of the present invention are capable of inhibiting angiogenesis and tumor growth. Thus, it is respectfully submitted that such a teaching in Zhang et al. in no way negates this surprising finding by the Applicants. In other words, Zhang et al. does not demonstrate that the claimed peptides consisting of sequences at least 90% identical to amino acids 13-39 and 111-136 of HARP lack the requisite functional activity.

Similarly, US 6,103,880 does not teach any peptide consisting of sequences at least 90% identical to amino acids 13-



39 and 111-136 of HARP that does not exhibit angiogenesis inhibiting activity.

Therefore, the references relied upon by the Office in making the rejection do not negate the Applicants' surprising finding that the claimed peptide fragments contain the requisite functionality.

For these reasons, it is respectfully submitted that the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, could construct any of the limited number of peptides encompassed by the new claims and then use the assays disclosed in the specification in order to confirm that such peptides have the requisite angiogenesis inhibiting activity and a capacity for binding to the ALK receptor without undue experimentation.

Therefore, withdrawal of the above-noted enablement rejection is solicited.

Turning now to the written description rejection.

The test for sufficiency of written description is whether the disclosure reasonably conveys to the artisan that the inventor had possession at the time of filing of the subject matter which is claimed. See M.P.E.P. § 2163, I, 2100-159, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph.

This test may be satisfied by: (1) a reduction to practice; (2) a reduction to drawings/chemical formulas; (3) a disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms; (4) a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure; (5) a sufficient description of a representative number of species; or (6) a combination of the above, sufficient to show the inventors were in possession of the invention. See M.P.E.P. § 2163,II, A, 3a(i)-(ii).

In the instant case, the Office has acknowledged that the specification clearly discloses isolated peptides consisting of SEQ ID NO: 2 or SEQ ID NO: 3, and compositions comprising the isolated peptide consisting of SEQ ID NO: 2, and SEQ ID NO: 3, or SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4.

It is respectfully submitted that such peptides constitute a reduction practice, a disclosure of a representative number of species and a clear reduction to drawings/chemical formulas of the invention.

Further, as noted above, the new claims are directed to peptides consisting of a sequence at least 90% identical to SEQ ID NOs: 2, 3 or 4. As such, the new claims relate to peptides consisting of a limited number of specific fragments of the HARP factor, and comprising at most three differences compared to SEQ

ID NOs: 2, 3 and 4. The specification at page 7, line 30 to page 8, line 14 also discusses which mutations within SEQ ID NOs: 2, 3 and 4 are expected not to abolish the biological activity of the peptides.

It is respectfully submitted that this constitutes a sufficient disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms. It also amounts to a sufficient disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure.

In view of the above, one of skill in the art would reasonably believe that Applicants were in possession of the claimed invention at the time of filing. Therefore, withdrawal of the above written description rejection is solicited.

#### **VII. INDEFINITENESS REJECTION**

Claims 10 and 16 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the reasons in item 19 on page 14 of the Action.

The claims have been amended to remedy the stated bases of rejection. It is noted that the new claims correspond to the language suggested by the Office at the bottom of page 14 of the Office Action.

With respect to the rejected phrase "associated with" in old claim 16, this language refers to a non-covalent association. More specifically, the embodiment on page 18, lines 13-17 teaches that the peptides of the invention may be present within two separate compositions that are administered simultaneously to an individual. This embodiment therefore rules out a covalent association between the peptides of the inventions. This interpretation is reinforced by Example 4 on page 28, lines 8-11, in which two peptides according to the invention are administered to a mouse as a mixture. Nonetheless, for the sole purpose of expediting prosecution, kindly note that the term "associated" has been replaced with the phrase "is combined" in new claim 36 (old claim 16).

Therefore, withdrawal of the above rejection is solicited.

#### **VIII. ANTICIPATION REJECTIONS**

In item 21 on page 15 of the Office Action, claim 2 was rejected under 35 U.S.C. § 102(b) as anticipated by Hampton et al.

In item 22 on page 15, claim 2 was rejected under 35 U.S.C. § 102(b) as anticipated by Backer et al. (US 5,461,029).

In item 23 on page 16, claims 1-3, 15-16 and 19 were rejected under 35 U.S.C. § 102(b) as anticipated by WO 02/083851.

These rejections are addressed together below.

The rejections were based on the premise that claims 1 and 2 contained the open-ended "comprising format", and as such, they read on the larger reference peptides. The present amendment removes this concern as old claim 1 has been cancelled and replaced with new independent claim 20. New claim 20 is in "consisting of" format, and therefore does not read on the reference peptides.

For this reason, the isolated peptide of independent claim 20 is novel and unobvious over the cited references. The remaining claims directly or indirectly depend on claim 20. Accordingly, these claims are also novel and unobvious for the same reasons due to their dependency on claim 20. Withdrawal of the rejections is therefore solicited.

Further, with respect to WO 02/083851, the Examiner alleges that SEQ ID NO: 36 (AAE32362) of WO 02/083851 corresponds to a peptide consisting of a sequence 100% identical to SEQ ID NO: 3 of the present invention. In reply, kindly note that SEQ ID NO: 36 of WO 02/083851 corresponds to amino acids 65-118 of HARP, and not to amino acids 65-97 of HARP as is the case for SEQ ID NO: 3. Further, since the new claims are drawn to peptides consisting of an amino acid sequence at least 90% identical to SEQ ID NO: 3, they are novel and unobvious over WO 02/083851.

Lastly, no other sequence of WO 02/083851 has been identified that would be identical to SEQ ID NO: 3 of the present

invention, and there appears to be a typographical error in AAE32362, which corresponds to a fifteen amino acid long sequence disclosed in US patent No. 5,968,817.

#### **IX. OBVIOUSNESS REJECTION**

In item 26 on pages 17-18, claims 1 and 8-9 were rejected under 35 U.S.C. § 103(a) as obvious over WO 200283851 in view of Barritault et al. (US 6,103,880) and/or Bernard-Pierrot et al.

It is respectfully submitted that the present amendment overcomes the 103(a) rejection for the same reasons set forth immediately above. Nothing in the cited references discloses or suggests the particular limited number of peptides of the claims. Withdrawal of the rejection is solicited.

#### **X. CONCLUSION**

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. An early notice to that effect is hereby requested.


If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Charge the fee of \$50 for the one claim of any type added herewith, to our credit card set forth in the attached Credit Card Payment Form.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

  
\_\_\_\_\_  
Jay F. Williams, Reg. No. 48,036  
209 Madison Street, Suite 500  
Alexandria, VA 22314  
Telephone (703) 521-2297  
Telefax (703) 685-0573  
(703) 979-4709

JFW/fb

**APPENDIX:**

The Appendix includes the following items:

- Substitute Specification (clean and marked-up copies);
- Copies of references cited in the IDS of May 2, 2005.